UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

10/MAR/2010

MEMORANDUM

Subject:	Name of Pesticide Product:	Fluroxypyr Meptyl TGAI
	EPA File Symbol:	35935-TU
	DP Barcode:	D371426
	Decision No.:	401100
	Action Code:	R310
	PC Codes:	128968 (fluroxypyr 1-methylheptyl ester)

From: Eugenia McAndrew, Biologist
Technical Review Branch
Registration Division (7505P)

To: Dianne Morgan, RM Team 23
Herbicide Branch
Registration Division (7505P)

Applicant: Nufarm Americas, Inc.
150 Harvester Drive, Suite 200
Burr Ridge, Illinois 60527

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Fluroxypyr 1-methylheptyl ester	97.8
Inert Ingredient(s):	2.2
Total:	100.0%

ACTION REQUESTED: The Risk Manager requests review of acute toxicity data submitted for EPA File Symbol 35935-TU.

BACKGROUND: Nufarm Americas, Inc. has submitted a six pack of acute toxicity studies to support the registration of the proposed product, Fluroxypyr Meptyl TGAI, EPA File Symbol 35935-TU. The studies were conducted at Eurofins/Product Safety Laboratories, Inc. and were assigned MRID numbers 478887-01 to -04 and 478997-01 and -02. A CSF dated October 8, 2009 for a basic formulation is included in the submission. An Agency contractor, Oak Ridge National Laboratory, conducted the primary review of the studies. TRB performed the secondary review and made changes as necessary.

RECOMMENDATIONS: The six studies are classified as acceptable.

The acute toxicity profile for Fluroxypyr Meptyl TGAI, EPA File Symbol 35935-TU, is as follows:

Acute oral toxicity	III	Acceptable	MRID 47888701
Acute dermal toxicity	III	Acceptable	MRID 47888702
Acute inhalation toxicity	IV	Acceptable	MRID 47888703
Primary eye irritation	IV	Acceptable	MRID 47888704
Primary skin irritation	IV	Acceptable	MRID 47899701
Dermal sensitization	Negative	Acceptable	MRID 47899702

LABELING: Based on the toxicity profile above, the following are the precautionary and first aid statements for the proposed product as obtained from the Label Review System:

PRODUCT ID #: 035935-00074

PRODUCT NAME: Fluroxypyr Meptyl TGAI

PRECAUTIONARY STATEMENTS

SIGNAL WORD: CAUTION

Hazards to Humans and Domestic Animals:

Harmful if absorbed through skin. Harmful if swallowed. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Remove and wash contaminated clothing before reuse.

First Aid:

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

DATA EVALUATION RECORD

FLUROXYPYR 1-METHYLHEPTYL ESTER
(FLUROXYPYR MEPTYL TECHNICAL, NUP-08211)

STUDY TYPE: ACUTE ORAL TOXICITY - RAT [OPPTS 870.1100; OECD 425]
ACUTE DERMAL TOXICITY - RAT [OPPTS 870.1200; OECD 402]
ACUTE INHALATION TOXICITY - RAT [OPPTS 870.1300; OECD 403]
ACUTE EYE IRRITATION - RABBIT [OPPTS 870.2400; OECD 405]
ACUTE DERMAL IRRITATION - RABBIT [OPPTS 870.2500; OECD 404]
DERMAL SENSITIZATION (LOCAL LYMPH NODE ASSAY) - MOUSE [OECD 429]

MRID 47888701, 47888702, 47888703, 47888704, 47899701, and 47899702

Prepared for
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Prepared by
Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 1-35

Primary Reviewer:
Susan Chang, M.S.

Signature: S S Chang
Date: FEB 10 2010

Secondary Reviewers:
H. Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T.

Signature: Tim Borges
Date: FEB 10 2010

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date: FEB 10 2010

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L.A. Wilson
Date: FEB 10 2010

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

Reviewer: Eugenia McAndrew **Date:** March 10, 2010
Risk Manager (EPA): 23

STUDY TYPE: Acute Oral Toxicity – Rat; OPPTS 870.1100; OECD 425

TEST MATERIAL: Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508; off-white solid, soluble in water, acetone, methanol, ethyl acetate, dichloromethane, toluene, hexane)

CITATION: Oley, S. (2009) Fluroxypyr Meptyl Technical, NUP-08211 – Acute Oral Toxicity Up and Down Procedure in Rats. Study Number 27045. Eurofins/Product Safety Laboratories, 2394 US Highway 130, Dayton, NJ 08810. May 18, 2009. MRID 47888701.

SPONSOR: Nufarm Inc., 150 Harvester Drive, Suite 150, Burr Ridge, IL 60527

EXECUTIVE SUMMARY: In an acute oral toxicity study using the up and down method (MRID 47888701), five fasted, young adult female Sprague-Dawley rats (age: 9-10 weeks; body weight: 170-188 g; source: Ace Animals, Inc., Boyertown, PA) were given a single oral dose of Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508) as a 45% w/w solution in corn oil at a dose of 2000 mg/kg bw by gavage and observed for 14 days.

All animal survived, gained weight, and appeared active and healthy during the study. No gross abnormalities were noted at necropsy.

LD_{50} Females > 2000 mg/kg bw

Fluroxypyr Meptyl Technical, NUP-08211 is in EPA Toxicity Category III.

This study is classified as acceptable. It does satisfy the guideline requirements for an acute oral study (OPPTS 870.1100; OECD 425) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS AND DISCUSSION:

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: Monday, January 18, 2010, 5:58:04 PM
Data file name: 371426_work.dat
Last modified: 1/18/2010 5:58:02 PM

Test/Substance: Fluroxypyr Meptyl Technical, NUP-08211
Test type: Limit Test
Limit dose (mg/kg): 2000
Assumed LD_{50} (mg/kg): Default
Assumed sigma (mg/kg): 0.5

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	3101	2000	O	O
2	3102	2000	O	O
3	3103	2000	O	O
4	3104	2000	O	O
5	3105	2000	O	O

(X = Died, O = Survived)

Dose Recommendation: The limit test is complete.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
2000	5	0	5
All Doses	5	0	5

Statistical Estimates:

The LD_{50} is greater than 2000 mg/kg.

Animals were dosed as follows:

Animal Number	Sex	Dose Level (mg/kg)	Long-Term Outcome
3101	F	2000	S
3102	F	2000	S
3103	F	2000	S
3104	F	2000	S
3105	F	2000	S

S = Survival, D = Death

A. Mortality: All animals survived the study.

B. Clinical observations: All animals appeared active and healthy and gained weight throughout the study.

C. Gross necropsy: No gross abnormalities were noted in any animal at necropsy.

D. Note about test substance: From page 7 of the study report: Prior to use, the test substance was ground in a coffee mill. The ground test substance was administered as a 45% w/w mixture in corn oil. Preliminary solubility testing conducted by EPSL indicated mixtures in excess of 45% (i.e., 50-70%) were too viscous to be adminsiteerd properly.

E. Reviewer's conclusions: This reviewer agrees with the study author regarding the acute oral LD_{50}. Fluroxypyr Meptyl Technical, NUP-08211 is in EPA Toxicity Category III.

Reviewer: Eugenia McAndrew **Date:** March 10, 2010
Risk Manager (EPA): 23

STUDY TYPE: Acute Dermal Toxicity – Rat; OPPTS 870.1200; OECD 402

TEST MATERIAL: Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508; off-white solid, soluble in water, acetone, methanol, ethyl acetate, dichloromethane, toluene, hexane)

CITATION: Oley, S. (2009) Fluroxypyr Meptyl Technical, NUP-08211 – Acute Dermal Toxicity in Rats –Limit Test. Study Number 27046. Eurofins/Product Safety Laboratories, 2394 US Highway 130, Dayton, NJ 08810. May 19, 2009. MRID 47888702.

SPONSOR: Nufarm Inc., 150 Harvester Drive, Suite 150, Burr Ridge, IL 60527

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 47888702), five male and five female young adult Sprague-Dawley rats (age: 8 weeks; body weight: males: 205-224 g and females: 181-200 g; source: Ace Animals, Inc., Boyertown, PA) were dermally exposed on an area of approximately 2 inches x 3 inches (approximately 10% of the total body surface area) of the clipped dorsal trunk for 24 hours to 2000 mg/kg bw Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508). Prior to application, the test material was moistened with distilled water to prepare a 65% w/w mixture (dry paste) applied to a gauze pad, and placed on the shaved trunk. The gauze and the trunk were wrapped with Durapore tape. The animals were observed for 14 days.

All animals survived, gained weight, and appeared active and healthy during the study. No gross abnormalities were noted at necropsy.

LD_{50} Males > 2000 mg/kg bw
LD_{50} Females > 2000 mg/kg bw
LD_{50} Combined > 2000 mg/kg bw

Fluroxypyr Meptyl Technical, NUP-08211 is in EPA Toxicity Category III.

This study is classified as acceptable. It does satisfy the guideline requirements for an acute dermal study (OPPTS 870.1200; OECD 402) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS AND DISCUSSION:

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
2000	0/5	0/5	0/10

A. **Mortality:** All animals survived the study.

B. **Clinical observations:** All animals gained weight and appeared active and healthy during the study.

C. **Gross necropsy:** No gross abnormalities were noted at necropsy.

D. **Reviewer's conclusions:** This reviewer agrees with the study author regarding the acute dermal LD_{50}. Fluroxypyr Meptyl Technical, NUP-08211 is in EPA Toxicity Category III.

Reviewer: Eugenia McAndrew **Date:** March 10, 2010
Risk Manager (EPA): 23

STUDY TYPE: Acute Inhalation Toxicity – Rat; OPPTS 870.1300; OECD 403

TEST MATERIAL: Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508; off-white solid, soluble in water, acetone, methanol, ethyl acetate, dichloromethane, toluene, hexane)

CITATION: Oley, S. (2009) Fluroxypyr Meptyl Technical, NUP-08211 – Acute Inhalation Toxicity Study in Rats. Study Number 27047. Eurofins/Product Safety Laboratories, 2394 US Highway 130, Dayton, NJ 08810. May 18, 2009. MRID 47888703.

SPONSOR: Nufarm Inc., 150 Harvester Drive, Suite 150, Burr Ridge, IL 60527

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 47888703), five male and five female young adult Sprague-Dawley rats (age: 8-9 weeks old; body weight: males: 230-248 g and females: 176-202 g; source: Ace Animals, Inc., Boyertown, PA) were exposed by nose-only inhalation to Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508) for 4 hours and 1 minute at a concentration of 2.09 mg/L. The test substance was aerosolized as received. The animals were observed for 14 days. The MMAD was 4.0 and 3.8 μm and the GSD 2.35 and 2.37 at 1.5 and 3 hours, respectively.

All animals survived, gained weight, and appeared active and healthy during the study. No gross abnormalities were noted at necropsy.

LC_{50} Males > 2.09 mg/L
LC_{50} Females > 2.09 mg/L
LC_{50} Combined > 2.09 mg/L

Fluroxypyr Meptyl Technical, NUP-08211 is in EPA Toxicity Category IV.

This study is classified as acceptable. It does satisfy the guideline requirements for an acute inhalation study (OPPTS 870.1300; OECD 403) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS AND DISCUSSION:

Nominal Conc. (mg/L)	Gravimetric Conc. (mg/L)	MMAD µm	GSD	Mortality/Number Tested		
				Males	Females	Combined
12.06	2.09	4.0, 3.8	2.35, 2.37	0/5	0/5	0/10

Test Atmosphere / Chamber Description: The test material was aerosolized using a Wright Dust Generator driven by a variable speed motor. The test material was packed into the dust container and compressed at 250 lbs/inch^2. The container was fitted with a stainless steel cutting head and cutting blade. Filtered air was supplied by an air compressor to the dust generator at 30 psi. Additional compressed mixing air from a compressed air tank was introduced into the chamber to help uniformly distribute the test atmosphere. The aerosolized dust was fed directly into the chamber through the dust outlet assembly. The exposure chamber was a Mini Nose-Only Inhalation Chamber (ADG Development Ltd.) with an internal volume of approximately 6.7 L. Animals were individually housed in polycarbonate holding tubes sealed to the chamber during exposure.

Gravimetric Conc. (mg/L):	**2.09**
Chamber Volume (L):	**6.7**
Total Airflow (L/min):	**31.7**
Temperature	**20-22°C**
Relative Humidity	**33-36%**
Time to equilibrium:	**1 minute**

Test atmosphere concentration: During exposure, gravimetric samples were collected six times from the breathing zone of the animals, using glass fiber filters. Filter papers were weighed before and after collection to determine the mass collected. The value was divided by the total volume of air sampled to determine the chamber concentration.

Particle size determination: Particle size was determined twice using an eight-stage Andersen cascade impactor. The test material concentration collected at each stage was determined gravimetrically. The mass median aerodynamic diameter and geometric standard deviation were determined graphically using two-cycle logarithmic probit axes.

A. Mortality: All animals survived the study.

B. Clinical observations: All animals appeared active and healthy and gained weight during the study.

C. Gross necropsy: No gross abnormalities were noted at necropsy.

D. Reviewer's conclusions: This reviewer agrees with the study author regarding the acute inhalation LC_{50}. Fluroxypyr Meptyl Technical, NUP-08211 is in EPA Toxicity Category IV.

Reviewer: Eugenia McAndrew **Date:** March 10, 2010
Risk Manager (EPA): 23

STUDY TYPE: Primary Eye Irritation – Rabbit; OPPTS 870.2400; OECD 405

TEST MATERIAL: Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508; off-white solid, soluble in water, acetone, methanol, ethyl acetate, dichloromethane, toluene, hexane)

CITATION: Oley, S. (2009) Fluroxypyr Meptyl Technical, NUP-08211 – Primary Eye Irritation Study in Rabbits. Study Number 27048. Eurofins/Product Safety Laboratories, 2394 US Highway 130, Dayton, NJ 08810. May 18, 2009, Amended March 9, 2010. MRID 47888704.

SPONSOR: Nufarm Inc., 150 Harvester Drive, Suite 150, Burr Ridge, IL 60527

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 47888704), 0.1 mL (0.06 g) of Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508; pH not reported) was instilled into the conjunctival sac of the right eye of three female young adult New Zealand White rabbits (source: Robinson Services, Inc., Clemmons, NC). The untreated eye served as a control. The test substance was ground in a coffee mill. Prior to instillation, 2-3 drops of ocular anesthetic (Tetracaine Hydrochloride Ophthalmic Solution, 0.5%) were placed into both the treated and control eye of each animal. The animals were observed for 72 hours.

A score of 1 was noted for conjunctivitis in one eye at the one hour observation resolving by 24 hours. No corneal opacity, iritis, or positive conjunctival irritation was noted on any rabbit during the study.

In this study, the formulation was minimally irritating. Fluroxypyr Meptyl Technical, NUP-08211 is classified as EPA Toxicity Category IV for primary eye irritation.

This study is classified as acceptable. It does satisfy the guideline requirements for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS AND DISCUSSION:

	Number "positive"/Number treated			
	Hours			
Observations	**1**	**24**	**48**	**72**
Corneal Opacity	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3
Conjunctivae:				
Redness*	0/3	0/3	0/3	0/3
Chemosis*	0/3	0/3	0/3	0/3
Discharge**	0/3	0/3	0/3	0/3

* Score of 2 or more required to be considered "positive"
** Discharge is not a positive effect according to the grading scale

A. **Observations:** A score of 1 was noted for conjunctivitis in one eye at the one hour observation resolving by 24 hours. No corneal opacity, iritis, or positive conjunctival irritation was noted on any rabbit during the study.

B. **Results:** Fluroxypyr Meptyl Technical, NUP-08211 was minimally irritating. The highest maximum mean total score was 4.0, recorded one hour after test material instillation (system of Kay and Calandra).

C. **Reviewer's conclusions:** This reviewer agrees with the study author that the test material was minimally irritating. Fluroxypyr Meptyl Technical, NUP-08211 is classified as EPA Toxicity Category IV for primary eye irritation.

Reviewer: Eugenia McAndrew **Date:** March 10, 2010
Risk Manager (EPA): 23

STUDY TYPE: Primary Dermal Irritation – Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL: Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508; off-white solid, soluble in water, acetone, methanol, ethyl acetate, dichloromethane, toluene, hexane)

CITATION: Oley, S. (2009) Fluroxypyr Meptyl Technical, NUP-08211 – Primary Skin Irritation Study in Rabbits. Study Number 27049. Eurofins/Product Safety Laboratories, 2394 US Highway 130, Dayton, NJ 08810. May 19, 2009. MRID 47899701.

SPONSOR: Nufarm Inc., 150 Harvester Drive, Suite 150, Burr Ridge, IL 60527

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 47899701), three female young adult New Zealand White rabbits (source: Robinson Services, Inc., Clemmons, NC) were dermally exposed to 0.5 g of Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508; pH not reported) for 4 hours. The test material was moistened with distilled water to prepare a 65% w/w mixture (dry paste). The test mixture (0.77 g) was placed on a gauze pad and applied on a 6 cm^2 area of the clipped dorsal skin. The pad and trunk were wrapped with semi-occlusive Micropore tape. Elizabethan collars were placed on the rabbits. The coverings and collars were removed after exposure. The animals were observed and dermal irritation was scored at 1, 24, 48, and 72 hours.

No dermal irritation was noted on any animal during the study.

In this study, the formulation was not irritating based on the Primary Irritation Index (PII) = 0.0. Fluroxypyr Meptyl Technical, NUP-08211 is classified as EPA Toxicity Category IV for primary dermal irritation.

This study is classified as acceptable. It does satisfy the guideline requirements for a primary dermal irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS AND DISCUSSION:

Animal Number	Sex	Hours			
		1	24	48	72
3501	F	0/0[a]	0/0	0/0	0/0
3502	F	0/0	0/0	0/0	0/0
3503	F	0/0	0/0	0/0	0/0
Severity of Irritation – Mean Score		0.0	0.0	0.0	0.0

[a] Erythema/edema

A. **Observations:** No dermal irritation was noted on any animal during the study.

B. **Results:** Fluroxypyr Meptyl Technical, NUP-08211 was not irritating. The Primary Irritation Index (PII) is 0.0.

C. **Reviewer's conclusions:** This reviewer agrees with the study author that the test material was not irritating. Fluroxypyr Meptyl Technical, NUP-08211 is classified as EPA Toxicity Category IV for primary dermal irritation.

Reviewer: Eugenia McAndrew **Date:** March 10, 2010
Risk Manager (EPA): 23

STUDY TYPE: Dermal Sensitization (Local Lymph Node Assay) – mouse; OPPTS 870.2600; OECD 429

TEST MATERIAL: Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508; off-white solid, soluble in water, acetone, methanol, ethyl acetate, dichloromethane, toluene, hexane)

CITATION: Oley, S. (2009) Fluroxypyr Meptyl Technical, NUP-08211 – Local Lymph Node Assay (LLNA) in Mice. Study Number 27050. Eurofins/Product Safety Laboratories, 2394 US Highway 130, Dayton, NJ 08810. May 18, 2009. MRID 47899702.

SPONSOR: Nufarm Inc., 150 Harvester Drive, Suite 150, Burr Ridge, IL 60527

EXECUTIVE SUMMARY: In a local lymph node assay study (MRID 47899702) with Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508), groups of five female CBA/J mice (age: 12 weeks; body weight: 20.0-24.2 g; source: Jackson Labs) group received 25 µL of the test material administered topically to the dorsal surface of each ear once daily for 3 consecutive days at 0 (negative control: acetone/olive oil 4:1), 25, 50, or 75% test material or 25% HCA (positive control) in acetone/olive oil 4:1, respectively. On day 6, the mice were injected intravenously with 250 µL of sterile phosphate buffered saline (PBS) containing 20 µCi of ^{3}H-thymidine/mouse via the tail vein. ^{3}H-thymidine – incorporation into the auricular lymph node DNA was measured and expressed as the number of disintegrations per minute (dpm). A stimulation index (SI) was derived for each group by dividing the mean dpm of each group by the mean dpm of the vehicle control group. A positive response was indicated by an SI of ≥3.0.

No statistically significant increases in cell proliferation measurement compared to the vehicle control group were observed at any test concentration. The SIs were 1.17, 1.28, and 2.18 for 25%, 50%, and 75% test material, respectively. The SI was 6.06 for the positive control.

Based on the results of this study, Fluroxypyr Meptyl Technical, NUP-08211 did not produce a dermal sensitization response in mice.

This study is classified as acceptable. It does satisfy the guideline requirements for a skin sensitization study (OECD 429).

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

PROCEDURE:

MATERIALS AND METHODS:

A. **Vehicle and positive control**: Acetone/olive oil 4:1 v/v was the vehicle. The positive control was α–hexylcinnamaldehyde (HCA) in acetone/olive oil 4:1 v/v.

B. **Treatment preparation and administration**: The dermal sensitization potential of the test material was examined using the local lymph node assay (LLNA). Fluroxypyr Meptyl Technical, NUP-08211 was combined with acetone/olive oil 4:1 v/v to obtain concentrations of 25%, 50%, and 75%. Groups of five female CBA/J mice received 25 µL of the test material administered topically to the dorsal surface of each mouse ear once daily for 3 consecutive days at 0 (negative control: acetone/olive oil 4:1 v/v), 25, 50, or 75% test material or 25% HCA in acetone/olive oil 4:1 v/v, respectively. On day 6, the mice were injected intravenously with 250 µL of sterile phosphate buffered saline (PBS) containing 20 µCi of ^{3}H-thymidine/mouse via the lateral tail vein. Approximately 5 hours after the injection, the animals were killed. The auricular lymph nodes were excised and placed in PBS, washed, and single cell suspensions were prepared. The cells were pelletted at 1750 rpm for approximately 10 minutes and the supernatant was decanted and discarded. This process was carried out twice. The pellet was re-suspended in 5 mL 5% TCA. After approximately18 hour incubation at 4°C, the precipitates were recovered and centrifuged and re-suspended in 1 mL of TCA and transferred to a scintillation vial containing 10 mL of scintillation fluid. The ^{3}H-thymidine – incorporation was measured in a beta-scintillation and expressed as the number of disintegrations per minute (dpm). Determination of radioactivity was performed individually on each animal. A stimulation index (SI) was derived for each group by dividing the mean dpm of each group by the mean dpm of the vehicle control group. A positive response was indicated by a SI of ≥3.0.

RESULTS AND DISCUSSION:

A. **Disintegrations per Minute (group means)**:

Concentration %	Group Mean DPM	Stimulation Index (SI)[#]
Vehicle	500.97	N/A
25% Fluroxypyr Meptyl Technical, NUP-08211	588.03	1.17
50% Fluroxypyr Meptyl Technical, NUP-08211	642.66	1.28
75% Fluroxypyr Meptyl Technical, NUP-08211	1094.31	2.18
25% HCA positive control	3034.92*	6.06

* significantly different from control group $p<0.01$

B. Stimulation Index:

Sample Description Test or Control	Vehicle	Low	Medium	High	Positive Control
Stimulation Index	N/A	1.17	1.28	2.18	6.06

C. Reviewer's conclusion: This reviewer agrees with the study author that the test material was not a dermal sensitizer.

D. Reference: None

1. **DP BARCODE:** DP371426
2. **PC CODE:** 128968
3. **CURRENT DATE:** March 10, 2010
4. **TEST MATERIAL:** Fluroxypyr Meptyl Technical, NUP-08211 (Fluroxypyr meptyl, 98.1%; Batch No. 20070508; off-white solid, soluble in water, acetone, methanol, ethyl acetate, dichloromethane, toluene, hexane)

Study/Species/Lab Study # / Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat Eurofins/Product Safety Laboratories 27045/May 18, 2009	47888701	LD_{50} > 2000 mg/kg bw females	III	A
Acute dermal toxicity/rat Eurofins/Product Safety Laboratories 27046/May 19, 2009	47888702	LD_{50} > 2000 mg/kg bw males, females combined	III	A
Acute inhalation toxicity/rat Eurofins/Product Safety Laboratories 27047/May 18, 2009	47888703	LC_{50} > 2.09 mg/L males, females combined	IV	A
Primary eye irritation/rabbit Eurofins/Product Safety Laboratories 27048/May 18, 2009	47888704	Minimally irritating	IV	A
Primary dermal irritation/rabbit Eurofins/Product Safety Laboratories 27049/May 19, 2009	47899701	Not irritating	IV	A
Dermal sensitization (Local lymph node assay)/mouse Eurofins/Product Safety Laboratories 27050/May 18, 2009	47899702	Not sensitizing	-	A

Core Grade Key: A = Acceptable, S = Supplementary, U = Unacceptable, W = Waived